

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please delete the Sequence Listing starting on page 74 and insert the accompanying Sequence Listing after the Abstract.

Please replace the first paragraph on page 10 with the following paragraph:

Corresponding results were achieved on administration of CpG DNA before, after and simultaneously with the mRNA vaccination described above. CpG represents a relatively rare dinucleotide sequence in DNA, in which the cytosine residue is often methylated, so that 5-methylcytosine is present. The methylation of the cytosine residue has effects on gene regulation, such as e.g. inhibition of the binding of transcription factors, blockade of promoter sites etc.). That is to say, here also not only was there an increased Th2 immune response, but moreover a Th1 immune response was induced. Here also, particularly good results were achieved if the CpG DNA was administered approximately 24 hours after administration of the mRNA according to the invention. In particular, CpG DNA with the motif CpG DNA 1668 with the sequence 5'-TCC ATG ACG TTC CTG ATG CT-3' (SEQ ID NO:1) or the motif CpG 1982 5'-TCC AGG ACT TCT CTC AGG TT-3' (SEQ ID NO:2) was used in the experiments.

Please replace the paragraph beginning in the middle of page 31 with the following paragraph:

In a further preferred embodiment of the present invention, the A/U content in the environment of the ribosome binding site of the modified mRNA from step (a.) and/or step (b.) of the method

according to the invention is increased compared with the A/U content in the environment of the ribosome binding site of the particular wild-type mRNA. This modification (an increased A/U content around the ribosome binding site) increases the efficiency of ribosome binding to the mRNA according to the invention. An effective binding of the ribosomes to the ribosome binding site (Kozak sequence: GCCGCCACCAUGG, (SEQ ID NO:3) the **AUG** forms the start codon) in turn has the effect of an efficient translation of the mRNA according to the invention or of the other abovementioned mRNAs having adjuvant properties.

Please replace the paragraph beginning in the middle of page 34 with the following paragraph:

The mRNA from step (a.) and/or step (b.) of the method according to the invention furthermore preferably has at least one 5' and/or 3' stabilizing sequence. These stabilizing sequences in the 5' and/or 3' untranslated regions have the effect of increasing the half-life of the mRNA according to the invention in the cytosol. These stabilizing sequences can have a 100 % sequence homology to naturally occurring sequences which occur in viruses, bacteria and eukaryotes, but can also be partly or completely synthetic in nature. The untranslated sequences (UTR) of the β -globin gene, e.g. from *Homo sapiens* or *Xenopus laevis* may be mentioned as an example of stabilizing sequences which can be used in the present invention. Another example of a stabilizing sequence has the general formula (C/U)CCAN_xCCC(U/A)PyUC(C/U)CC (SEQ ID NO:4), which is contained in the 3'UTR of the very stable mRNA which codes for α -globin, α -(I)-collagen, 15-lipoxygenase or for tyrosine hydroxylase (cf. Holcik et al., Proc. Natl. Acad. Sci. USA 1997, 94: 2410 to 2414). Such stabilizing sequences can of course be used


individually or in combination with one another and also in combination with other stabilizing sequences known to a person skilled in the art. The mRNA from step (a.) and/or step (b.) of the method according to the invention is therefore preferably present as globin UTR (untranslated regions)-stabilized mRNA, in particular as β -globin UTR-stabilized mRNA. It has been found, according to the invention, that injection of naked β -globin UTR (untranslated regions)-stabilized mRNA according to the invention, optionally in combination with adjuvant mRNA likewise modified in such a manner or otherwise, into the ear pinna of a mammal (e.g. of mice) induces a specific immune response to the antigen which is coded by the mRNA according to the invention (17). In other words, the inventors have monitored and investigated the course of the injected β -globin UTR-stabilized mRNA and the type of immune response which it triggers and have thus detected a translation *in vivo* (see Figure 1). This vaccination strategy has been investigated further, and a pharmaceutical mRNA which can be used in human clinical trials has been developed.

Please replace the first paragraph on page 46 with the following paragraph:

Figure 3c: The cytotoxic activity of splenocytes which were cultured in the presence of purified β -galactosidase for six days was checked in a chromium release assay. The target cells were P815 ($H2^d$) cells, which were either charged (■) with the synthetic peptide TPHPARIGL (SEQ ID NO:5), which corresponds to the dominant $H2-L^d$ epitope of β -galactosidase, or were not charged (□).

Please replace the first and second paragraphs under the diagram on page 49 with the following paragraphs:

 Xenopus β -globin 5' Untranslated region:
GCTTGTCTCTTTTGCAGAAGCTCAGAATAAACGCTCAACTTTGGC (SEQ ID NO:6)

 Xenopus β -globin 3' untranslated region:
GACTGACTAGGATCTGGTTACCACTAAACCAGCCTCAAGAACACCCGAATGGAG
TCTCTAAGCTACATAATAACCACTTACACTTACAAAATGTTGTCCCCCAAAATG
TAGCCATTTCGTATCTGCTCCTAATAAAAAGAAAGTT TCTTCACATTCTA
(SEQ ID NO:7)
or
human α -globin untranslated Region:
CTAGTGACTGATAGCCCGCTGGGCCTCCCAACGGGCCCTCCTCCCCCTCCTTGCA
CC (SEQ ID NO:8)